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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,358	02/05/2004	William Stern	P/546-279 REISSUE	8408

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NEW YORK, NY 100368403

EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,358	STERN, WILLIAM	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/06 & 10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Remarks and IDS filed on 09/28/06, an IDS filed on 10/03/06 and a letter, summary of the Interview filed on 11/13/06. No claims were amended, cancelled or added. Accordingly claims 13-44 remain pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims **13-18, 20-21, 24-44** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claims 13, 24, 41 and 42 the new range of 10-25mM is considered new matter because the specification does not have support for the said range. The Provisional Application of 60/180,241 also has no support for the said range.

Claims **13-18, 20-21, 24-44** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The term "the aggregate

concentration of all such bioavailability..." is considered new matter. There is no support for the said term in the specification.

The rejection of claims 13-18, 20-21, 24-44 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is **withdrawn** per Applicant's statement that the range for osmotic pressure of from 250 to 350 mOsm/liter was disclosed in the parent application and the provisional application. Applicants have stated that the said range will be added to the instant specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-14, 17-18, 20-23, 34, 38, 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Chiodini et al (5,719,122).

Chiodini et al disclose pharmaceutical compositions comprising a **calcitonin** and a polyglycolysed glyceride and a method of enhancing the transmucosal absorption of calcitonin. Calcitonin may be a natural or synthetic calcitonin. Human, **salmon** and eel calcitonins are the most preferred types (see col. 2, line 50 to col. 4, line 19). The said polyglycolysed glycerides which are suitable for the said formulations include

polyethylene glycol esters such as Labrasol™ and Gelucire 44/14™ (see col. 2, lines 19-34). The **nasal** formulations are typically in solution, gel, drops or **aerosol** forms (see col. 5, lines 14-16). The **pH** of the composition is suitably at a range of from 3 to 8, preferably **3.5 to 7**. A buffering agent such as citrates, for example a mixture of citric acid and sodium citrate is employed to adjust the pH levels (see col. 6, lines 13-25). Example 19 discloses a solution formulation for nasal or buccal administration. The total amount of the citrates used in the said formulation is about 18 mM. Other ingredients may be used in the said formulations such as polyhydroxy alcohols such as propylene glycol; excipients such as parabens and benzyl alcohol, agents for adjusting viscosity, agents for adjusting tonicity, etc (see col. 5, lines 52-65).

Claims 13-14, 17, 20-23, 34, 40-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Grebow et al (5,026,825).

Grebow et al teaches an **intranasal** formulations comprising **calcitonin** and excipients. The **salmon** and chicken calcitonins have a potency of about 4,000 to 6,000 MCR U/mg peptide (col. 3, lines 4-15). The said formulations may be administered across the **nasal membranes** as a spray, nose drop or aerosol (col. 11, lines 15-21).

Grebow also discloses that the nasal spray solutions are especially preferred with water or in a buffer at a **pH of between 3.0 and 8.0** using a buffer system including a mixture of sodium citrate and citric acid in the range of **0.01 M to 0.5 M**. This concentration was found effective to **provide stability** of the dissolved calcitonin in the diluent base or vehicle (col. 11, lines 35-47). Furthermore the formulations are said to

have been made in 0.2M buffer at a pH value of 4.1 (col. 14, lines 34-35). The preparations may also comprise other additives including stabilizers, tonicity adjusters, viscosity builders, preservatives and the like (col. 11, lines 48-52). The said additives include methyl paraben, propyl paraben, phenethyl alcohol, etc. Grebow discloses certain suitable concentration ranges of the said additives in the table of column 12.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 15-16, 18-19, 24-33, 35-39 and 43-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grebow et al (5,026,825) as applied to claims 13-14, 17, 20-23, 34, 40-42 above, and further in view of Azria et al (5,733,569).

Grebow et al, discussed above, lacks specific disclosure on the osmolality and viscosity of the formulations.

Azria et al discloses galenic compositions comprising calcitonin for nasal administration. Azria discloses that preferred **pH** levels for a nasal formulation is from 3 to 5 or most preferably from **3.5 to 4.5**. The formulation also should have an appropriate isotonicity and viscosity. Preferably the osmotic pressure is from **about 260 to about**

380 mOsm/l and the desired viscosity is from 2 to about $40x10^{-3}$ Pa.S or more preferably less than $2x10^{-3}$ Pa.s (see col. 4, lines 13-28).

It would have been obvious to one of ordinary skill in the art given the nasal solution formulations of Grebow et al to have looked in the art for suitable osmolality and viscosity for intranasal administration as taught by Azria et al, for ultimate effectiveness and safety. It is clearly stated by Azria et al and other prior art references and well known in the art that for delivery to sensitive mucosa such as nasal, eye, ear, etc, specific ranges in osmolality, isotonicity and viscosity are required. Thus one of ordinary skill in the art would have been motivated to have made certain the required properties are present in a formulation for nasal administration. In other words the combination of references provides sufficient information to one of ordinary skill in the art to make and use the invention as claimed.

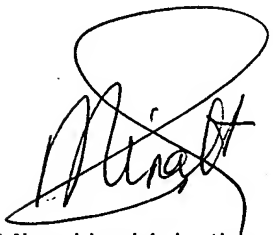
Response to Arguments

Applicant's arguments with respect to claims 13-44 filed on 09/28/06 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 571-272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Mina Haghighatian
Patent Examiner
March 01, 2007